SYNOPSIS

Design and Synthesis of Biologically Active Nitrogen and Sulfur Containing Heterocyclic Compounds and its Novel Derivatives

Submitted to

Swami Ramanand Teerth Marathwada University, Nanded

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FOR THE AWARD OF THE DEGREE OF

DOCTOR OF PHILOSOPHY

IN

CHEMISTRY

By

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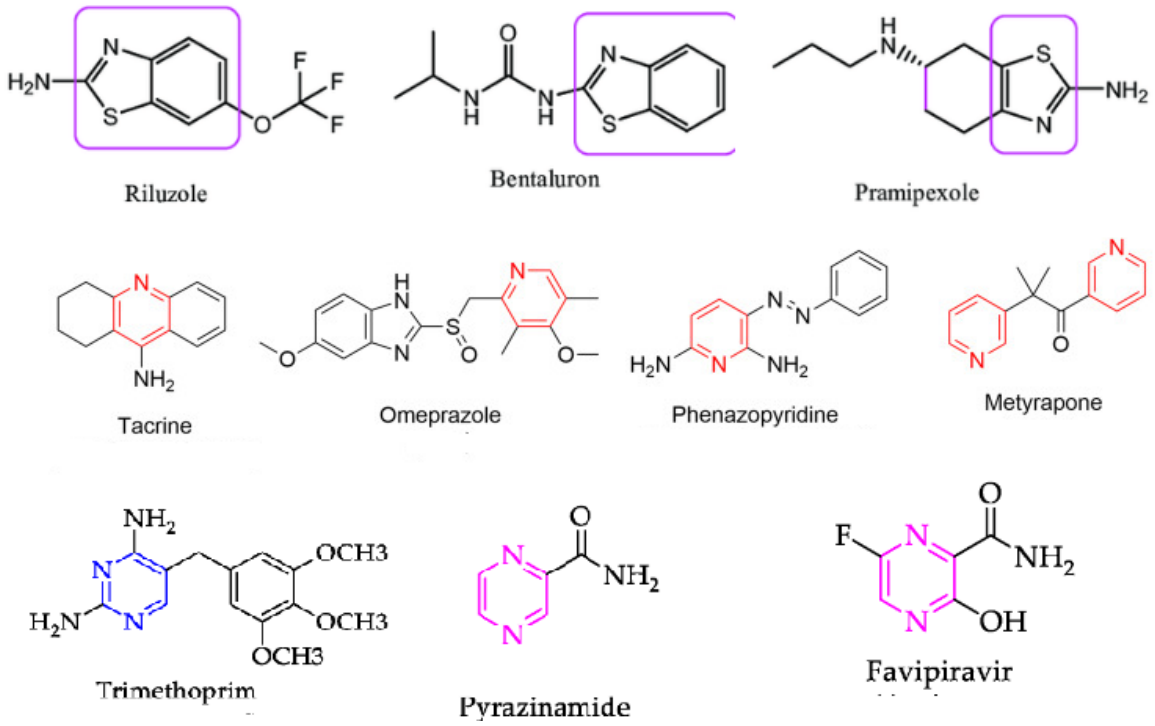
SYNOPSIS

Title of the proposed research:

Design and Synthesis of Biologically Active Nitrogen and Sulfur Containing Heterocyclic Compounds and its Novel Derivatives

Introduction:

Heterocycles have constituted one of the largest areas of research in organic chemistry. Nearly 80% of medications used in clinical settings have a heterocyclic composition. Heterocycles play on important role in biochemistry processes because the side groups of the most typical and essential constituents of living cells, DNA and RNA are based on aromatics heterocycles [1],Heterocyclic moiety is found as a key structural element in a number of therapeutic medication categories, including analgesic, anti-convulsant, anti-inflammatory, anti-hypertensive, anti-malarial, anti-depressant, anti-histaminic, anti-proliferative, and antidiabeticetc [2]. Along with multistep synthesis, synthesis via one pot or multicomponent reactions (MCRs) have also gain substantial scope due to powerful bond forming effectiveness in combinatorial and medicinal chemistry [3]. Heterocycles are completely interlinked into the life processes. Among theheterocycles, the Piperazine, Substituted Piperazine and Pyrimidine occupy a prominent position. They possess a broad range of biological activities and are found in many potent biologically active molecules and drugs such as vitamin thiamine, sulfathiazol (antimicrobial drug), ritonavir (antiretroviral drug) [4,5], abafungin (antifungal drug) and tiazofurin (antineoplastic drug).Heterocyclic compounds are the cyclic organic compounds which contain at least one hetero atom, the most common heteroatom's are the nitrogen, oxygen and Sulphur atoms are widely known[6,7].Medicinal chemistry is the science that deals with the discovery and design of new therapeutic chemicals and their development into useful medicines [8, 9]. Following are some heterocyclic derivatives present in drugs-



Literature Survey:

From the literature survey it is observed that, the many heterocyclic compounds are shows antiproliferative activity to different degrees, it's difficult to predict which combination of group acts on which type of target [10, 11]. Prediction about their activity is difficult, in present time there is lot of research is happening on anticancer agents, basically we have to treat the kinases /enzymes in the body for the effective treatment of cancer [12, 13]. Presently all the research is focused on different kinases as these plays a key role in the cancer metabolism and functions of normal body cells [14]. The analogs of nitrogen and sulfur based heterocycles occupy an exclusive position as a valuable source of therapeutic agents in medicinal chemistry. More than 75% of drugs approved by the FDA and currently available in the market are nitrogen and sulfur containing heterocyclic moieties [1 to 10]. Heterocyclic nuclei offer a huge area for new lead molecules for drug discovery and for generation of activity relationships with biological targets for enhance pharmacological effects.

Need and significance:

The development in chemotherapy of synthetic drugs totally depends upon the biological results of chemotherapeutic agents which ultimately give the guidelines to the research workers in selection of agents for further clinical studies and set the pattern of future drug evaluation. Considering literature survey, the fusion of two or more heterocyclic nuclei

such as thiazole,benzthiazole pyridine, pyrimidine indazole Piperazine, etc are in combination enhances the biological profile many fold than parent nuclei, Thiazole moiety is a prevalent scaffold in a number of naturally occurring and synthetic molecules with attractive biological activities such as antiviral, anticancer, antibacterial, antifungal, anticonvulsant, and anti-inflammatory activities that is well illustrated by the large number of drugs in the market containing this heterocyclic moiety. The different heterocyclic derivative s possesses different biological activity it's difficult to predict which combination groups acts on which diseases, so constant research is needed.

Aims and Objectives of the research:

The main objectives of the proposed work includes,

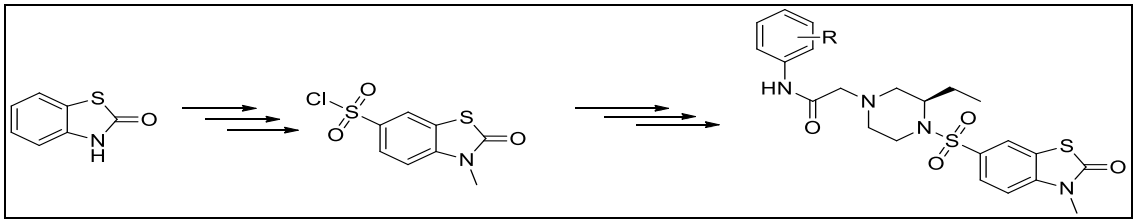
1. To synthesize new series of nitrogen and sulfur containing Benzthaizole, pyrimidin and pyridine heterocycles.
2. To characterize newly synthesized compounds by modern spectral techniques
3. Biological testing such as antibacterial, antifungal, antiviral, antiproliferative activity and kinase study of synthesized compounds.

Methodology:

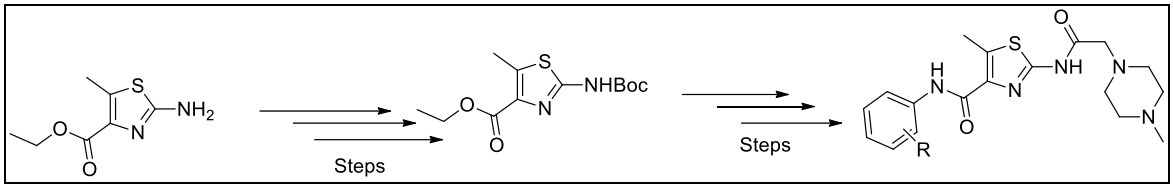
Considering the objectives synthesis of target molecule will be carried out with different starting materials such as Benzthaizole, pyridine, pyrimidine substituted piperazine etc, through a series of reactions and there sulfonamide, amide and acetamide derivative.. Attempt will be made to optimize existing methodology or to develop new method for synthesis of series. The synthesized compounds of above class will be then tested for related biological activity using in-vitro assay. The techniques like UV, IR, 1H NMR, 13C NMR Spectroscopy will be used for the structural determination of the synthesized compounds.

Part A: Synthesis of Piperazine substituted Benzthaizole and Thaizole derivatives.

1. Synthesis of Acetamide derivatives of (R)-6-((2-ethylpiperazin-1-yl)sulfonyl)-3-methylbenzo[d]thiazol-2(3H)-one.

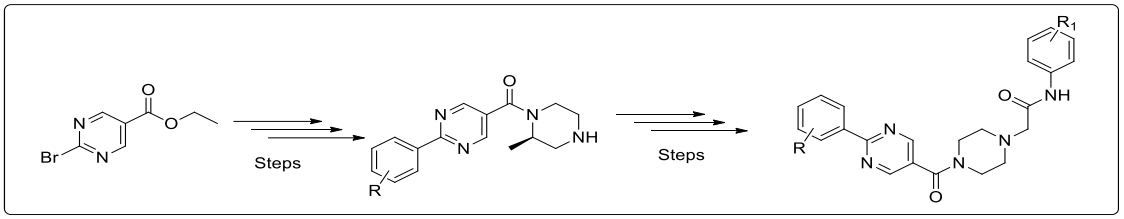


2. Synthesis of sulphonamide derivatives of 5-methyl-2-(2-(4-methylpiperazin-1-yl)acetamido)thiazole-4-carboxylic acid

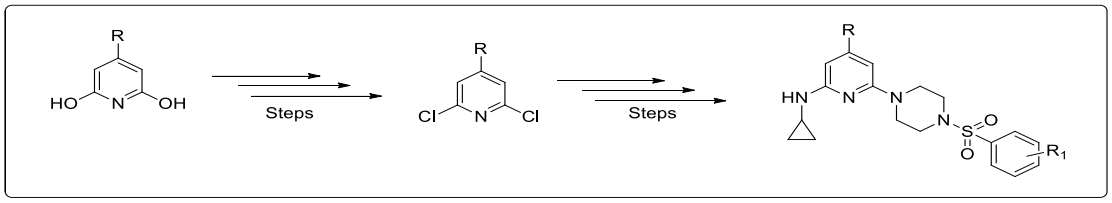


Part B: Synthesis of Piperazine substituted Pyrimidine and Pyridine derivatives.

3. Synthesis of Acetamide derivatives of (R)-(2-methylpiperazin-1-yl)(2-phenylpyrimidin-5-yl)methanone.



4. Synthesis of 2, 6-dichloro-4-(trifluoromethyl) pyridine and there substituted piperazine Sulphonamide derivatives.



Plan of Research

Year	Quarters (Periods of three months)	Milestones
Year I	1st Quarter	Reference Work
	2nd Quarter	Topic first literature survey
	3rd Quarter	Topic second Experimental Work and characterization

	4th Quarter	Topic second Experimental Work and characterization
Year II	1 st Quarter	Topic third Experimental Work and characterization
	2nd Quarter	Topic third Experimental Work and characterization
	3rd Quarter	Topic Fourth Experimental Work and characterization
	4th Quarter	. Topic Fourth Experimental Work and characterization
Year III .	1 st Quarter	Topic Fifth Experimental Work and characterization
	2nd Quarter	Topic sixth Biological evaluation
	3rd Quarter	Topic sixth Biological evaluation
	4th Quarter	Writing and typing of the research work and submission of the research work

Hypothesis:

Literature search and design of bioactive molecules. The synthesize of designed analogues, having different combinations of heterocycles. Antimicrobial, Antifungal, Antiproliferative and kinase activity testing of designed molecules

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